

REMARKS

Rejection of Claims Under 35 U.S.C. 102

Claims 1-4 and 31 stand rejected under 35 U.S.C. 102 for allegedly being anticipated by U.S. Patent No. 6,406,498 to Tormala (the '498 patent). Applicants traverse this rejection. Claim 1 recites a multifunctional synthetic bioabsorbable device comprising solid particles of a pharmacological agent. The Examiner states that according to U.S. Patent No. 6,579,533, bioactive glass is anti-bacterial and thus the bioactive glass is considered a pharmaceutical agent. Bioactive glasses belong to a group of bioceramics that are used as biomaterials (See Exhibit A). Although some bioactive glasses have anti-bacterial properties, they are not considered "pharmacological agents" as that term is understood by one in the art. "Pharmacological" is an adjective derived from the word "pharmacology," which according to the New Oxford Dictionary of English (Clarendon Press, Oxford 1998) is "the branch of medicine concerned with the uses, effects and modes of action of drugs." (See Exhibit B). Bioactive glasses are biomaterials not drugs. As such, a bioactive glass is not a "pharmacological agent" as recited in claim 1. Accordingly, Applicants submit that claim 1 (and all claims that depend therefrom) are not anticipated by the '498 patent and Applicants request withdrawal of this rejection.

Rejection of Claims Under 35 U.S.C. 103

Claims 1-26 and 31 stand rejected as being allegedly rendered obvious by EP 1157708 to Fischer ("Fischer") in view of the '498 patent. Fischer states that antimicrobial agents should not undergo chemical degradation or modification, or loss of anti-microbial properties under processing conditions. (See *e.g.* page 3, lines 22-24). However, there is no teaching or suggestion that the a pharmacological agent should retain its solid particulate form in the melt-processing of the matrix as recited in claim 1. Therefore, it would not be obvious to produce a multi-functional bioabsorbable device which comprises a pharmaceutical agent and cavities around the solid particles of the pharmaceutical agent dispersed in a synthetic bioabsorbable oriented polymer matrix as recited by claim 1. Accordingly, Applicants submit that claim 1 (and all claims that depend therefrom) are not rendered obvious by the combination of the '498 patent and Fischer and Applicants request withdrawal of this rejection.

Conclusion

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees that are required in connection with the filing of this response are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon LLP Deposit Account No. 11-0600.

Respectfully submitted,

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/Zeba Ali/
Zeba Ali
Reg. No. 51,392

Kenyon & Kenyon LLP
1500 K Street, N.W., Suite 700
Washington, D.C. 20005
Telephone: (202) 220-4200
Facsimile: (202) 220-4201

Bioceramics

Larry L. Hench*

Department of Materials, Imperial College of Science, Technology, and Medicine, University of London, London, United Kingdom

Ceramics used for the repair and reconstruction of diseased or damaged parts of the musculo-skeletal system, termed bioceramics, may be bioinert (e.g., alumina and zirconia), resorbable (e.g., tricalcium phosphate), bioactive (e.g., hydroxyapatite, bioactive glasses, and glass-ceramics), or porous for tissue ingrowth (e.g., hydroxyapatite-coated metals). Applications include replacements for hips, knees, teeth, tendons, and ligaments and repair for periodontal disease, maxillofacial reconstruction, augmentation and stabilization of the jaw bone, spinal fusion, and bone repair after tumor surgery. Pyrolytic carbon coatings are thromboresistant and are used for prosthetic heart valves. The mechanisms of tissue bonding to bioactive ceramics have resulted in the molecular design of bioceramics for interfacial bonding with hard and soft tissue. Bioactive composites are being developed with high toughness and elastic modulus that match with bone. Therapeutic treatment of cancer has been achieved by localized delivery of radioactive isotopes via glass beads. Clinical success of bioceramics has led to a remarkable advance in the quality of life for millions of people.

I. Introduction

MANY millennia ago, the discovery that fire would irreversibly transform clay into ceramic pottery led to an agrarian society and an enormous improvement in the quality and length of life. Another revolution has occurred in the use of ceramics during the past four decades to improve the quality of life. This revolution is the innovative use of specially designed ceramics for the repair, reconstruction, and replacement of diseased or damaged parts of the body. Ceramics used for this purpose are termed "bioceramics." Bioceramics can be polycrystalline (alumina or hydroxyapatite), bioactive glass, bioactive

glass-ceramic (A/W), or bioactive composite (polyethylene-hydroxyapatite).

Many specialty ceramics and glasses have been developed during this century for use in the health care industry, e.g., eyeglasses, diagnostic instruments, chemical ware, thermometers, tissue culture flasks, fiber optics for endoscopy, and carriers for enzymes and antibodies.¹ Ceramics also are used widely in dentistry as restorative materials, gold porcelain crowns, glass-filled ionomer cements, dentures, etc. The materials used in these applications are called dental ceramics.²

This review is devoted to the use of bioceramics as implants to repair parts of the body, usually the hard tissues of the musculo-skeletal system, such as bones, joints, or teeth, although use of carbon coatings for replacement of heart valves also is included. Many ceramic compositions have been tested for use in the body;³ however, few have achieved human clinical application. Clinical success requires the simultaneous achievement of a stable interface with connective tissue and a match of the mechanical behavior of the implant with the tissue to be replaced. Only the few bioceramics that meet these severe requirements for clinical success are emphasized in this review. Historical developments of bioceramics have been presented by Hulbert *et al.*⁴

(1) Need for Bioceramics

Bioceramics are needed to alleviate pain and restore function to diseased or damaged parts of the body. A major contributor to the need for "spare parts" for the body is the progressive deterioration of tissue with age. Bone is especially vulnerable to fracture in older people because of a loss of bone density and strength with age.⁵ Figure 1 summarizes the effect of time on bone strength and density from the age of 30 years onward. The effect is especially severe in women because of hormonal changes associated with menopause. Bone density decreases because bone-growing cells (osteoblasts) become progressively less productive in making new bone and repairing microfractures. The lower density greatly deteriorates the strength of the porous bone, called trabecular or cancellous bone (Fig. 2), in the ends of long bones and in vertebrae. An unfortunate consequence is that many old people fracture their hips or have collapsed vertebrae and spinal problems.

The great challenge facing the use of ceramics in the body is to replace old, deteriorating bone with a material that can func-

P. W. Brown—contributing editor

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*Member, American Ceramic Society.

centennial feature

pharmaceutical

The Pharmaceus are mentioned only by Josephus and in the Talmud. Unlike the Sadducees, who had no law, the Pharisees law was strictly the Pharisees' own. The Pharisees were the most numerous of the sects. Although in the Gospels they are mentioned as the chief opponents of Christ they were in fact the only party in the Synagogue to the present Church, with which they stand united in the Pharisees.

DERIVATIVES *pharmaceutic* [fɑr'meʃu'tɪk] *adjective*
Pharmaceutical adjective, Pharmaceutic [fɑr'meʃu'tɪk] *adjective*

ORIGIN Old English *farmas*, via ecclesiastical Latin from Greek *pharmakos* from *pharmakē* 'medicine' 'separated ones' (related to Hebrew *pharis* 'separated').

pharmaceutical [fɑr'meʃu'tɪk] *adjective* or relating to medicinal drugs, their preparation, use, or sale.

pharmaceutical [fɑr'meʃu'tɪk] *noun* (usu. *pharmaceuticals*) a compound manufactured or used as a medicinal drug.

pharmaceutical [fɑr'meʃu'tɪk] *noun* a company manufacturing medicinal drugs.

DERIVATIVES *pharmaceutically* *adverb*, *pharmaceutician* *noun*

ORIGIN mid 17th cent.: via late Latin from Greek *pharmaceutikos* from *pharmakos* 'druggist', from *pharmakon* 'drug'.

pharmacist [fɑr'meʃu'tɪk] *noun* a person who is professionally qualified to prepare and dispense medicinal drugs.

pharmaceutic [fɑr'meʃu'tɪk] *adjective* relating to drugs; *pharmaceutically* *adverb*.

pharmacodynamics [fɑr'meʃu'tɪk] *noun* (usu. *pharmacodynamics*) the branch of pharmacology concerned with the effects of drugs and the mechanism of their action.

pharmacogenetics [fɑr'meʃu'tɪk] *noun* (usu. *pharmacogenetics*) the branch of pharmacology concerned with the effect of genetic factors on reactions to drugs.

pharmacognosy [fɑr'meʃu'tɪk] *noun* (usu. *pharmacognosy*) the branch of knowledge concerned with medicinal drugs obtained from plants or other natural sources.

pharmacologist [fɑr'meʃu'tɪk] *noun* a person who is professionally qualified to prepare and dispense medicinal drugs.

pharmacokinetics [fɑr'meʃu'tɪk] *noun* (usu. *pharmacokinetics*) the branch of pharmacology concerned with the movement of drugs within the body.

pharmacology [fɑr'meʃu'tɪk] *noun* the branch of medicine concerned with the uses, effects, and modes of action of drugs.

pharmacological [fɑr'meʃu'tɪk] *adjective*, *pharmacologically* *adverb*, *pharmacologist* *noun*

ORIGIN early 18th cent.: from modern Latin *pharmacologia*, from Greek *pharmakon* 'drug'.

pharmacopoeia [fɑr'meʃu'tɪk] *noun* (usu. *pharmacopoeia*) a book especially an official publication, containing a list of medicinal drugs with their effects and directions for their use.

ORIGIN early 17th cent.: modern Latin, from Greek *pharmakopoiia* 'art of preparing drugs', based on *pharmakon* 'drug' + *poiia* 'making'.

pharmaceutical [fɑr'meʃu'tɪk] *noun* (usu. *pharmaceutical*) medical treatment by means of drugs.

pharmacy [fɑr'meʃu'tɪk] *noun* (usu. *pharmacy*) a shop or hospital dispensary where medicinal drugs are provided or sold.

pharmaceutical [fɑr'meʃu'tɪk] *noun* the science or practice of the preparation and dispensing of medicinal drugs.

ORIGIN late Middle English (denoting the administration of drugs) from Old French *farmacie*, via medieval Latin from Greek *pharmakia* 'practice of the druggist', based on *pharmakon* 'drug'.

Pharos [fɑr'meʃu'tɪk] *noun* a lighthouse, often considered one of the Seven Wonders of the World, erected by Ptolemy II (ruled 283-262 BC) on the island of Pharos, off the coast of Alexandria.

pharos [fɑr'meʃu'tɪk] *noun* a lighthouse or a beacon to guide ships.

pharyngeal [fɑr'meʃu'tɪk] *adjective* or relating to the pharynx.

pharyngeal [fɑr'meʃu'tɪk] *noun* (usu. *pharyngeal*) a feature of the root of the tongue with the pharynx, a feature of certain consonants in Arabic, for example.

pharyngeal [fɑr'meʃu'tɪk] *noun* a feature of the root of the tongue with the pharynx, a feature of certain consonants in Arabic, for example.

ORIGIN early 19th cent.: from modern Latin

pharyngeus [fɑr'meʃu'tɪk] *noun* (usu. *pharyngeus*) 'throat' + *-us*.

pharyngeal [fɑr'meʃu'tɪk] *adjective* (also *-al*) relating to the pharynx.

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phase diagram [fɑz 'di:grəm] *noun* Chemistry a diagram representing the limits of stability of the phases in a chemical system at equilibrium with respect to variables such as composition and temperature.

phase-locked [fɑz 'lɒkəd] *adjective* (usu. *phase-locked*) (usu. *phase-locked*) a device that maintains a stable oscillator of lower frequency by means of a phase difference generated by any shift in frequency.

phase modulation [fɑz 'mɒdʒuːlən] *noun* (usu. *phase modulation*) a variation of the phase of a radio or other wave means of carrying information such as a signal.

phaser [fɑzə] *noun* an instrument that alters a signal by phasing it. (In science fiction) a weapon that delivers a lethal gas or anoxia.

phase rule [fɑz 'ruːl] *noun* Chemistry a rule relating possible numbers of phases, consisting degrees of freedom in a chemical system.

phase shift [fɑz 'ʃɪft] *noun* Physics a change in the phase of a waveform.

phase space [fɑz 'speɪs] *noun* Physics a multidimensional space in which each axis corresponds to a coordinate required to specify the state of a physical system, all the coordinates being represented so that a point in the space corresponds to a state of the system.

phase velocity [fɑz 'veləːsəti] *noun* Physics the speed of propagation of a sine wave, or a wave component of a complex wave, equal to the product of its wavelength and frequency.

phasic [fɑzɪk] *adjective* or relating to a phase.

phasic [fɑzɪk] *noun* (usu. *phasic*) a phase of a cycle, or a phase of a cycle.

phasing [fɑzɪŋ] *noun* (usu. *phasing*) the relationship between the timing of two or more events, or the adjustment of a system to a given state.

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